

REMARKS

Applicant respectfully requests entry of the amendments and reconsideration of the claims. Claim 1 has been amended to further clarify the claimed subject matter. Support for the amendment can be found at page 4, lines 26 to 27. Applicants have added new claims 21-25. Support can be found throughout the specification, including at pages 12-14. Claims 1-3, 19, and 21-25 will be pending upon entry of the amendment. Applicant respectfully requests reconsideration and withdrawal of the rejections under 35 U.S.C. § 103(b) and § 112, first paragraph.

Applicant also wishes to remind the Examiner of co-pending application serial number 10/761,596, which is a continuation of the instant application.

Examiner Interview

Applicants are grateful for the grant and time spent on a personal interview between Mr. David Heller, Applicants' representatives, and Mark Williams (Director of Product Development at DiaMedica, Inc.) with Examiner Charlesworth Rae and Supervisor Brian Kwon. The pending rejection under 35 U.S.C. § 103(a) was discussed.

Rejection under 35 U.S.C. § 103(a)

The Examiner rejects claims 1-3 and 19 as allegedly obvious over Adams et al. (U.S. Patent 6,165,975; already made of record) in view of Lautt et al. (U.S. Patent 5,561,165). Applicant respectfully traverses.

To make a *prima facie* case of obviousness, the teachings of the prior art should have suggested the claimed subject matter to the person of ordinary skill in the art, and all the claim limitations must be taught or suggested in the references cited by the Examiner. *In re Kotzab*, 217 F.3d 1365, 1370 (Fed. Cir. 2000). As articulated by the Supreme Court in a recent case, a combination is obvious if it is no more than the predictable use of known elements according to their established functions; and there was a reason to combine the known elements. *KSR Int'l Co. v. Teleflex, Inc.*, 127 S. Ct. 1727 (2007). To make a *prima facie* case of obviousness, "it remains

necessary to identify the reason why a person of ordinary skill in the art would have combined the prior art elements in the manner claimed.” *Id.* Applicants submit that the Examiner does not make a *prima facie* case of obviousness because the Examiner has not established a reason to combine the known elements.

The Examiner cites the Adams et al. patent as teaching of method of treating a vascular condition (Office Action of May 16, 2007 at page 11, lines 3-4). Adams et al. disclose the "treatment of conditions concerned with peripheral vasoconstriction" (*See* Field of the Invention at col. 1, lines 12-13). Specifically, Adams et al. describe and claim methods of treating vascular tone to treat erectile and sexual dysfunctions (See col. 1, lines 16-21; claims; etc.). It is in this context that Adams et al. cite the passage the Examiner relies upon, that a "number of investigators have *postulated* that ET antagonists could be used for...diabetes..." (col. 2, lines 24-31; *emphasis added*).

"A prior art reference must be considered in its entirety, i.e., as a whole, including portions that would lead away from the claimed invention. MPEP § 2141.02(VI); *W.L. Gore & Associates, Inc. v. Garlock, Inc.*, 721 F.2d 1540 (Fed. Cir. 1983), *cert. denied*, 469 U.S. 851 (1984). Adams et al. postulate that endothelin inhibitors could treat a variety of disorders. All of the recited disorders are linked to hypertension. Adams et al., in its entirety, is concerned with peripheral vasoconstriction. Applicants respectfully assert that Adams et al. contemplate treating the hypertensive effects in the sub-population of diabetics (Type I and Type II) with hypertension and not the diabetes itself. Adams et al. do not suggest a treatment for insulin resistance in Type II diabetes. In viewing the teachings of Adams et al. in their entirety, Adams et al. suggest a treatment for diabetes related hypertension, but do not suggest a treatment for or connection with insulin sensitivity in Type II diabetes. There is no teaching or suggestion that the administration of NO donors would affect endothelin in any other context besides vasoconstriction/vasodilation. More specifically, there is no teaching or suggestion that NO donors alone, or by mediating endothelin expression, would increase insulin sensitivity. The Examiner has not provided a connection between NO donors and insulin sensitivity.

For at least these reasons, Applicants respectfully assert that there is no motivation to

combine the cited references, and thereby the Examiner has not established a *prima facie* case of obviousness. In view of the foregoing, Applicant respectfully requests reconsideration and withdrawal of the rejection under 35 U.S.C. § 103(a).

Summary

In view of the above amendments and remarks, the applicant respectfully requests a Notice of Allowance. If the Examiner believes a telephone conference would advance prosecution of this application, the Examiner is invited to telephone the undersigned at the below listed telephone number.

Respectfully submitted,

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